

CLAIMS

1. A method for improving vaccination comprising reactivation of the thymus of a patient.
2. The method of claim 1 wherein the patient's thymus has been at least in part
5 deactivated.
3. The method of claim 2 wherein the patient is post-pubertal.
4. The method of claim 1 further comprising the step of administering hematopoietic stem cells to the patient.
5. The method of claim 4 wherein the hematopoietic stem cells are CD34+.
- 10 6. The method of claim 4 wherein the hematopoietic stem cells are autologous or syngeneic.
7. The method of claim 4 wherein the hematopoietic stem cells are allogeneic or xenogeneic.
8. The method of claim 4 wherein the hematopoietic stem cells are administered
15 about the time when the thymus begins to regenerate or shortly thereafter.
9. The method of claim 4 wherein the hematopoietic stem cells are provided at the time disruption of sex steroid mediated signaling to the thymus is begun.
10. The method of claim 1 wherein the method of disrupting the sex steroid mediated signaling to the thymus is through surgical castration to remove the patient's gonads.
- 20 11. The method of claim 1 wherein the method of disrupting the sex steroid mediated signaling to the thymus is through administration of one or more pharmaceuticals.

12. The method of claim 11 wherein the pharmaceuticals are selected from the group consisting of LHRH agonists, LHRH antagonists, anti-LHRH vaccines and combinations thereof.

13. The method of claim 12 wherein the LHRH agonists are selected from the group
5 consisting of Eulexin, Goserelin, Leuprolide, Dioxalan derivatives, Triptorelin, Meterelin, Buserelin, Histrelin, Nafarelin, Lutrelin, Leuprorelin and Deslorelin.

14. The method of claim 1 resulting in a vaccine response by the patient's immune system that is comparable to the response of a pre-pubertal patient.

15. A method for improving an immune response to a vaccine antigen in a patient,
10 comprising:

reactivating the thymus of the patient; and

administering a vaccine to the patient, the vaccine comprising a vaccine antigen,

wherein the patient develops an immune response to the vaccine antigen.

16. The method of claim 15, wherein the thymus of the patient has been at least in
15 part atrophied before it is reactivated.

17. The method of claim 16, wherein the patient has a disease that at least in part atrophied the thymus of the patient.

18. The method of claim 16, wherein the patient has had a treatment of a disease that at least in part atrophied the thymus of the patient.

20 19. The method of claim 18, wherein the treatment is immunosuppression, chemotherapy, or radiation treatment.

20. The method of claim 16, wherein the patient is post-pubertal.

21. The method of claim 15, further comprising administering cells to the patient, wherein the cells are stem cells, progenitor cells, or combinations thereof.

22. The method of claim 21, wherein the stem cells are selected from the group consisting of hematopoietic stem cells, epithelial stem cells, and combinations thereof.

5 23. The method of claim 21, wherein the progenitor cells are selected from the group consisting of lymphoid progenitor cells, myeloid progenitor cells, and combinations thereof.

24. The method of claim 22, wherein the progenitor cells are selected from the group consisting of lymphoid progenitor cells, myeloid progenitor cells, and combinations thereof.

25. The method of claim 22, wherein the cells are hematopoietic stem cells.

10 26. The method of claim 25, wherein the hematopoietic stem cells are CD34+.

27. The method of claim 25, wherein the hematopoietic stem cells are autologous.

28. The method of claim 25, wherein the hematopoietic stem cells are not autologous.

29. The method of claim 25, wherein the hematopoietic stem cells are administered when the thymus begins to reactivate.

15 30. The method of claim 15, wherein the thymus is reactivated by disruption of sex steroid-mediated signaling to the thymus.

31. The method of claim 30, further comprising administering cells to the patient, wherein the cells are stem cells, progenitor cells, or combinations thereof.

20 32. The method of claim 31, wherein the stem cells are selected from the group consisting of hematopoietic stem cells, epithelial stem cells, and combinations thereof.

33. The method of claim 31, wherein the progenitor cells are selected from the group consisting of lymphoid progenitor cells, myeloid progenitor cells, and combinations thereof.

34. The method of claim 32, wherein the progenitor cells are selected from the group consisting of lymphoid progenitor cells, myeloid progenitor cells, and combinations thereof.

35. The method of claim 32, wherein the cells are hematopoietic stem cells.

36. The method of claim 35, wherein the hematopoietic stem cells are administered at
5 the time disruption of sex steroid-mediated signaling to the thymus is begun.

37. The method of claim 30, wherein the sex steroid-mediated signaling to the thymus is disrupted by surgical castration.

38. The method of claim 30, wherein the sex steroid-mediated signaling to the thymus is disrupted by chemical castration.

10 39. The method of claim 30, wherein the sex steroid-mediated signaling to the thymus is disrupted by administration of one or more pharmaceuticals.

40. The method of claim 39, wherein the one or more pharmaceuticals is selected from the group consisting of LHRH agonists, LHRH antagonists, anti-LHRH vaccines, anti-androgens, anti-estrogens, SERMs, SARMs, SPRMs, ERDs, aromatase inhibitors, anti-
15 progestogens, and combinations thereof.

41. The method of claim 40, wherein the LHRH agonists are selected from the group selected from the group consisting of Eulexin, Goserelin, Leuprolide, Dioxalan derivatives, Triptorelin, Meterelin, Buserelin, Histrelin, Nafarelin, Lutrelin, Leuprorelin, Deslorelin, Cystorelin, Decapeptyl, Gonadorelin, and combinations thereof.

20 42. The method of claim 40, wherein the LHRH antagonists are selected from the group consisting of Abarelix, Cetrorelix, and combinations thereof.

43. The method of claim 15, wherein patient's immune response to the vaccine antigen is improved compared to that immune response which would have otherwise occurred in a patient prior to thymus reactivation.

44. The method of claim 15, wherein the vaccine is a therapeutic vaccine or a prophylactic vaccine.

45. The method of claim 15, wherein the vaccine antigen is that of an agent selected from the group consisting of viruses, bacteria, fungi, parasites, prions, cancers, allergens,
5 asthma-inducing agents, "self" proteins and antigens which cause autoimmune disease.

46. The method of claim 45, wherein the agent is a virus.

47. The method of claim 46, wherein the virus is selected from the group consisting of Retroviridae, Picornaviridae, Calciviridae, Togaviridae, Flaviridae, Coronaviridae, Rhabdoviridae, Filoviridae, Paramyxoviridae, Orthomyxoviridae, Bungaviridae, Arenaviridae,
10 Reoviridae, Birnaviridae, Hepadnaviridae, Parvoviridae, Papovaviridae, Adenoviridae, Herpesviridae, Poxviridae, and Iridoviridae.

48. The method of claim 46, wherein the virus is selected from the group consisting of influenza virus, human immunodeficiency virus, and herpes simplex virus.

49. The method of claim 45, wherein the agent is a bacteria.

15 50. The method of claim 41, wherein the bacteria is selected from the group consisting of *Helicobacter pyloris*, *Borelia burgdorferi*, *Legionella pneumophilia*, *Mycobacteria tuberculosis*, *Mycobacteria. avium*, *Mycobacteria intracellulare*, *Mycobacteria kansaii*, *Mycobacteria gordonae*, *Mycobacteria* sporozoites, *Staphylococcus aureus*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Listeria monocytogenes*, *Streptococcus pyogene*,
20 *Streptococcus agalactiae*, *Streptococcus faecalis*, *Streptococcus bovis*, *Streptococcus pneumoniae*, pathogenic *Campylobacter* sporozoites, *Enterococcus* sporozoites, *Haemophilus influenzae*, *Bacillus anthracis*, *Corynebacterium diphtheriae*, *Corynebacterium* sporozoites, *Erysipelothrix rhusiopathiae*, *Clostridium perfringens*, *Clostridium tetani*, *Enterobacter aerogenes*, *Klebsiella pneumoniae*, *Pasturella multocida*, *Bacteroides* sporozoites,
25 *Fusobacterium nucleatum*, *Streptobacillus moniliformis*, *Treponema pallidum*, *Treponema pertenue*, *Leptospira*, and *Actinomyces israeli*.

51. The method of claim 49, wherein the bacteria is a mycobacteria.

52. The method of claim 45, wherein the agent is a parasite.

53. The method of claim 52, wherein the parasite is selected from the group consisting of *Plasmodium falciparum*, *Plasmodium yoelli*, and *Toxoplasma gondii*.

5 54. The method of claim 52, wherein the parasite is a malaria parasite.

55. The method of claim 45, wherein the agent is an infectious fungi.

56. The method of claim 55, wherein the infectious fungi is selected from the group consisting of *Cryptococcus neoformans*, *Histoplasma capsulatum*, *Coccidioides immitis*, *Blastomyces dermatitidis*, *Chlamydia trachomatis*, *Candida albicans*.

10 57. The method of claim 45, wherein the agent is a cancer or tumor.

58. The method of claim 57, wherein the cancer is selected from the group consisting of cancers of the brain, cancers of the lung, cancers of the ovary, cancers of the breast, cancers of the prostate, cancers of the colon, and cancers of the blood.

59. The method of claim 45, wherein the agent is an allergen.

15 60. The method of claim 59, wherein the allergen causes an allergic condition selected from the group consisting of eczema, allergic rhinitis, allergic coryza, hay fever, bronchial asthma, urticaria (hives), and food allergies.

61. The method of claim 45, wherein the patient was exposed to the agent prior to thymus reactivation.

20 62. The method of claim 45, wherein the patient was not exposed to the agent prior to thymus reactivation.

63. The method of claim 15, wherein the vaccine is selected from the group consisting of killed vaccines, inactivated vaccines, attenuated vaccines, recombinant vaccines, subunit vaccines, and DNA vaccines.

64. The method of claim 15, wherein the vaccine is administered when the thymus
5 begins to reactivate.

65. The method of claim 30, wherein the vaccine is administered at the time disruption of sex steroid-mediated signaling to the thymus is begun.

66. The method of claim 15, further comprising administering at least one cytokine, at least one growth factor, or a combination of at least one cytokine and at least one growth factor
10 to the patient.

67. The method of claim 66, wherein the cytokine is selected from the group consisting of Interleukin 2 (IL-2), Interleukin 7 (IL-7), Interleukin 15 (IL-15), and combinations thereof.

68. The method of claim 66, wherein the growth factor is selected from the group
15 consisting of members of the epithelial growth factor family, members of the fibroblast growth factor family, stem cell factor, granulocyte colony stimulating factor (G-CSF), keratinocyte growth factor (KGF), and combinations thereof.

69. The method of claim 67, wherein the growth factor is selected from the group consisting of members of the epithelial growth factor family, members of the fibroblast growth
20 factor family, stem cell factor, granulocyte colony stimulating factor (G-CSF), keratinocyte growth factor (KGF), and combinations thereof.

70. A method for delivering a sex steroid analog to a patient, comprising:

laser-irradiating the skin of the patient to create perforations or alterations in the skin,
and

25 placing the sex steroid analog on the irradiated skin,

wherein the sex steroid analog is delivered through the perforations or alterations in the irradiated skin.

71. A method for delivering a sex steroid analog to a patient, comprising:

delivering the sex steroid analog to the skin of the patient, and

5 permeabilizing the skin of the patient with high pressure impulse transients,

wherein the impulse transients cause the sex steroid analog to diffuse through the permeabilized skin of the patient.

72. A method for enhancing transplantation of donor hematopoietic stem cells into the thymus of a recipient patient, comprising:

10 depleting the T cells of the patient,

reactivating the thymus of the patient, and

transplanting donor hematopoietic stem cells to the patient,

wherein uptake of the donor hematopoietic stem cells into the patient's thymus is enhanced as compared to the uptake that would have otherwise occurred in a patient prior to
15 thymus reactivation.

73. A method for increasing virus-specific peripheral T cell responsiveness of a patient with an at least partially atrophied thymus, comprising:

reactivating the thymus of the patient,

exposing the patient to a virus,

20 determining the virus-specific peripheral T cell responsiveness in the patient,

wherein the patient has an increased viral-specific peripheral T cell responsiveness as compared to the responsiveness that would have otherwise occurred in a patient prior to thymus reactivation.